(FILE 'HOME' ENTERED AT 10:57:29 ON 10 MAR 2003)

FILE 'CAPLUS' ENTERED AT 10:57:40 ON 10 MAR 2003

		E	BALDRIDGE JORY/IN,AU
L1	12	S	E3-6
		E	JOHNSON DAVID A/IN,AU
L2	459	S	E2-15
		E	CLUFF CHRISTOPHER/IN,AU
L3	15	S	E2-8
		E	CLUFF CHRIS/IN,AU
L4	2	S	E2
L5	479	S	L1 OR L2 OR L3 OR L4
L6	1338	S	AGP
L7	11	S	AMINOALKYL GLUCOSAMINIDE
L8	25260	S	LPS
L9	4476	S	LIPID A
L10	29472	S	L6 OR L7 OR L8 OR L9
L11	21	S	L10 AND L5

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L11 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:90796 CAPLUS
TITLE: Immunostimulatory activity of **aminoalkyl glucosaminide** 4-phosphates (**AGPs**): Induction of protective innate immune responses by RC-524 and RC-529
AUTHOR(S): **Baldridge, Jory R.**; **Cluff, Christopher W.**; Evans, Jay T.; Lacy, Michael J.; Stephens, Jeffrey R.; Brookshire, Valerie G.; Wang, Rong; Ward, Jon R.; Yorgensen, Yvonne M.; Persing, David H.; **Johnson, David A.**
CORPORATE SOURCE: Corixa Corporation, Hamilton, MT, 59840, USA
SOURCE: Journal of Endotoxin Research (2002), 8(6), 453-458
CODEN: JENREB; ISSN: 0968-0519
PUBLISHER: Maney Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Earlier we showed that the structural requirements for adjuvanticity among the **aminoalkyl glucosaminide** 4-phosphate (**AGP**) class of synthetic immunostimulants may be less strict than those for other endotoxic activities, including the induction of nitric oxide synthase in murine macrophages and cytokine prodn. in human whole blood. The known role of nitric oxide and pro-inflammatory cytokines in the activation of host defenses against infection prompted us to examine the ability of certain **AGPs** to enhance non-specific resistance in mice to Listeria monocytogenes and influenza infections as well as to stimulate the prodn. of pro-inflammatory cytokines in mouse splenocytes, human PBMCs, and human U937 histiocytic lymphoma cells. Intranasal administration of RC-524 or RC-529 to mice 2 days prior to a lethal influenza challenge provided significant protection in each case. Similarly, the i.v. administration of these **AGPs** induced resistance to L. monocytogenes infection as measured by survival or redn. of bacteria in the spleen. Activation of the innate immune response by **AGPs** appears to involve activation of Toll-like receptor 4 (TLR4) because RC-524 failed to elicit a protective effect in C3H/HeJ mice which have a defect in TLR4 signaling or induce significant cytokine levels in C3H/HeJ splenocytes. Both **AGPs** also stimulated pro-inflammatory cytokine release in human cell cultures in a dose-dependent manner.
REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:759775 CAPLUS
DOCUMENT NUMBER: 137:261484
TITLE: Taking toll: **lipid A** mimetics as adjuvants and immunomodulators
AUTHOR(S): Persing, David H.; Coler, Rhea N.; Lacy, Michael J.; **Johnson, David A.**; **Baldridge, Jory R.**; Hershberg, Robert M.; Reed, Steven G.
CORPORATE SOURCE: Corixa, Seattle, WA, 98104, USA
SOURCE: Trends in Microbiology (2002), 10(10, Suppl.), s32-s37
CODEN: TRMIEA; ISSN: 0966-842X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Vaccine adjuvants based on the structure of **lipid A**, such as monophosphoryl **lipid A** (MLA), have proven to be safe and effective in inducing immune responses to heterologous proteins in animal and human vaccines. Recent work on the development of a recombinant vaccine for leishmaniasis has demonstrated that a clin. grade MLA formulation - MPL adjuvant - is essential in the development of a protective response. Preliminary evidence suggests that MLA and a chem. distinct family of **lipid A** mimetics - the **aminoalkyl glucosaminide** 4-phosphates - act on Toll-like receptor 4 (TLR4). As TLR4 agonists, they have potent immunomodulatory effects when used both as vaccine adjuvants and as stand-alone products. Novel approaches to vaccine development could benefit from taking full advantage of the effects of these compds. on innate and adaptive responses. Vaccine adjuvants based on the structure of **lipid A** have proven to be safe and effective in inducing immune responses to heterologous proteins in animal and human vaccines. Novel approaches to vaccine development could benefit from taking full advantage of the effects of these compds. on innate and adaptive responses.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:123023 CAPLUS
DOCUMENT NUMBER: 136:182448
TITLE: Aminoalkyl glycosaminide phosphate adjuvants
INVENTOR(S): **Johnson, David A.**; Baldridge, Jory; Sowell, Greg
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012258	A1	20020214	WO 2001-US24284	20010803
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001081001	A5	20020218	AU 2001-81001	20010803

PRIORITY APPLN. INFO.: US 2000-223056P P 20000804
WO 2001-US24284 W 20010803

AB The authors disclose the prepn., pyrogenicity, and immunostimulatory activity of a 2-deoxy-2-amino-.beta.-D-glucopyranose (glucosamine) glycosidically linked to a cyclic aminoalkyl (aglycon) group. An illustrative compd., RC-533, was shown to enhance both antibody and cytotoxic T-cell response to the surface antigen of hepatitis B virus.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:868475 CAPLUS
DOCUMENT NUMBER: 136:628
TITLE: Prophylactic and therapeutic treatment of infectious and other diseases with mono- and disaccharide-based compounds
INVENTOR(S): Persing, David H.; Crane, Richard Thomas; Elliot, Gary T.; Ulrich, J. Terry; Lacy, Michael J.; **Johnson, David A.**; **Baldridge, Jory R.**; Wang, Rong
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090129	A2	20011129	WO 2001-US16327	20010518
WO 2001090129	A3	20020606		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002077304	A1	20020620	US 2001-861466	20010518
EP 1284740	A2	20030226	EP 2001-948222	20010518
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2000-205820P P 20000519
US 2001-281567P P 20010404
WO 2001-US16327 W 20010518

OTHER SOURCE(S): MARPAT 136:628

AB Methods and compns. for treating or ameliorating diseases and other conditions, such as infectious diseases, autoimmune diseases and allergies are provided. The methods employ mono- and disaccharide-based compds. for selectively stimulating immune responses in animals and plants.

L11 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:757768 CAPLUS
DOCUMENT NUMBER: 135:302901
TITLE: **Aminoalkyl glucosaminide** phosphate compounds and their use as adjuvants and immunoeffectors
INVENTOR(S): **Johnson, David A.**; Sowell, C. Gregory
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: U.S., 44 pp., Cont.-in-part of U.S. 6,113,918.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6303347	B1	20011016	US 1999-439839	19991112
US 6113918	A	20000905	US 1997-853826	19970508
WO 2001034617	A2	20010517	WO 2000-US31340	20001113
WO 2001034617	A3	20011108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001019189	A5	20010606	AU 2001-19189	20001113
EP 1230250	A2	20020814	EP 2000-982119	20001113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2002045586	A1	20020418	US 2001-808669	20010314
US 2002048588	A1	20020425	US 2001-905160	20010712
NO 2002002207	A	20020710	NO 2002-2207	20020508

PRIORITY APPLN. INFO.:
US 1997-853826 A2 19970508
US 1991-815250 A 19911231
US 1998-138305 A1 19980821
US 1999-429238 A 19991028
US 1999-439839 A 19991112
US 1999-439849 B1 19991112
US 2000-190444P P 20000317
WO 2000-US31340 W 20001113

OTHER SOURCE(S): MARPAT 135:302901
AB **Aminoalkyl glucosaminide** phosphate (AGP) compds. that are adjuvants and immunoeffectors are described and claimed. The compds. have a 2-deoxy-2-amino glucose in glycosidic linkage with an aminoalkyl (aglycon) group. Compds. are phosphorylated at the 4 or 6 carbon on the glucosaminide ring and comprise three 3-alkanoyloxyalkanoyl residues. The compds. augment antibody prodn. in immunized animals as well as stimulate cytokine prodn. and activate macrophages. Methods for using the compds. as adjuvants and immunoeffectors are also disclosed.
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:713123 CAPLUS
DOCUMENT NUMBER: 135:267269
TITLE: Mono- and disaccharides for the treatment of nitric oxide related disorders
INVENTOR(S): Elliot, Gary; **Johnson, David**; Weber, Patricia A.; Sowell, Greg
PATENT ASSIGNEE(S): Corixa Corp., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2001070209	A2	20010927	WO 2001-US8513	20010315
WO 2001070209	A3	20020418		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1265620	A2	20021218	EP 2001-920455	20010315

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 2000-190444P	P	20000317
	WO 2001-US8513	W	20010315

OTHER SOURCE(S): MARPAT 135:267269

AB Methods for treating diseases or conditions modulated or ameliorated by nitric oxide, particularly ischemia and reperfusion injury, are provided, using glycolipids structurally related to monophosphoryl **lipid A** but with notable redn. in proinflammatory and pyrogenic activity.

L11 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:525947 CAPLUS
DOCUMENT NUMBER: 135:112005
TITLE: Composition of antigen and glycolipid adjuvant sublingual administration
INVENTOR(S): Wheeler, Alan; Elliott, Garry; **Cluff, Christopher Wallace**
PATENT ASSIGNEE(S): Allergy Therapeutics Limited, UK; Corixa Corporation
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001051082	A1	20010719	WO 2001-GB142	20010115

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

GB 2360210	A1	20010919	GB 2001-1035	20010115
EP 1255563	A1	20021113	EP 2001-942305	20010115

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	GB 2000-891	A	20000114
	WO 2001-GB142	W	20010115

AB A method of producing a mucosal and systemic immune response in a mammal comprising administering sublingually an effective amt. of a compn. comprising at least one antigen and a glycolipid adjuvant to said mammal. An example is given for prepn. of MPL (a form of 3 de-O-acylated monophosphoryl **lipid A**) adjuvant with DPPC.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:360008 CAPLUS
DOCUMENT NUMBER: 134:353474
TITLE: Preparation of **aminoalkyl glucosaminide** phosphates and their use as adjuvants and immuno-effectors
INVENTOR(S): **Johnson, David A.**; Sowell, C. Gregory
PATENT ASSIGNEE(S): Corixa Corporation, USA
SOURCE: PCT Int. Appl., 147 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034617	A2	20010517	WO 2000-US31340	20001113
WO 2001034617	A3	20011108		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6303347	B1	20011016	US 1999-439839	19991112
AU 2001019189	A5	20010606	AU 2001-19189	20001113
EP 1230250	A2	20020814	EP 2000-982119	20001113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
NO 2002002207	A	20020710	NO 2002-2207	20020508

PRIORITY APPLN. INFO.: US 1999-439839 A 19991112
US 1997-853826 A2 19970508
WO 2000-US31340 W 20001113

OTHER SOURCE(S): MARPAT 134:353474

AB **Aminoalkyl glucosaminide** phosphate compds. (**AGP**) I were prepd. wherein, X is selected from the group consisting of O and S at the axial or equitorial position; Y is selected from the group consisting of O and NH; Q is (CH2)n; L is (CH2)m; W is (CH2)q; n, m, p, q are integers from 0 to 6; R is (CH2)10Me; R1-R3 are the same or different and are normal fatty acyl residues having from 1 to about 20 carbon atoms and where one of R1-R3 is optionally hydrogen; R4 and R5 are the same or different and are selected from the group consisting of H and methyl; R6 and R7 are the same or different and are selected from the group consisting of H, hydroxy, alkoxy, phosphono, phosphonooxy, sulfo, sulfooxy, amino, mercapto, cyano, nitro, formyl and carboxy, and esters and amides thereof; and R8 and R9 are the same or different and are selected from the group consisting of phosphono and H, and at least one of R8 and R9 is phosphono, that are adjuvants and immuno-effectors are described and claimed. The compds. have a 2-deoxy-2-amino glucose in glycosidic linkage with an aminoalkyl (aglycon) group. Compds. are phosphorylated at the 4 or 6 carbon on the glucosaminide ring and comprise three 3-alkanoyloxyalkanoyl residues. The compds. augment antibody prodn. in immunized animals as well as stimulate cytokine prodn. and activate macrophages. Methods for using the compds. as adjuvants and immuno-effectors are also disclosed. Thus, N-[(R)-3-hydroxytetradecanoyl]-O-[2-deoxy-4-O-phosphono-2-[(R)-3-dodecanoyloxytetradecanoylamino]-3-O-[(R)-3-tetradecanoyloxytetradecanoyl]-.alpha.-L-D-glucopyranosyl]-L-serine triethylammonium salt was prepd. and tested in mice as adjuvants and immuno-effectors. Mice vaccinated with formalin-inactivated influenza and the **AGP** compds. of the subject invention mounted a protective immune response to an influenza challenge as well as produced antibody to that antigen.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:407550 CAPLUS

DOCUMENT NUMBER: 134:36798

TITLE: Monophosphoryl **lipid A** enhances mucosal and systemic immunity to vaccine antigens following intranasal administration

AUTHOR(S): **Baldridge, Jory R.**; Yorgensen, Yvonne; Ward, Jon R.; Ulrich, J. Terry

CORPORATE SOURCE: Ribi ImmunoChem Research Inc., Hamilton, MT, 59840, USA

SOURCE: Vaccine (2000), 18(22), 2416-2425
CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The induction of protective immunity stemming from vaccines delivered by mucosal routes is dependent on the development of safe and effective mucosal adjuvants. The immunostimulant monophosphoryl **lipid A** (MPL) was evaluated for its ability to enhance both systemic and mucosal immunity to three distinct antigens. Vaccines formulated with MPL and hepatitis B surface antigen, tetanus toxoid or influenza antigens were administered by intranasal delivery to mice. In each case the vaccines

formulated with MPL resulted in enhanced IgA titers from mucosal samples. Enhanced IgA concns. were detected in samples from both local and distal mucosal sites. In addn., the MPL formulated vaccines induced systemic immunity characteristic of a Th1-type of response. Serum IgG2a antibody titers were elevated and cytotoxic T cell activity was enhanced.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:769093 CAPLUS
DOCUMENT NUMBER: 132:137639
TITLE: Synthesis and biological evaluation of a new class of vaccine adjuvants: **aminoalkyl glucosaminide** 4-phosphates (**AGPs**). [Erratum to document cited in CA131:272113]
AUTHOR(S): **Johnson, David A.**; Sowell, C. Gregory; Johnson, Craig L.; Livesay, Mark T.; Keegan, David S.; Gustafson, Gary L.; Rhodes, Michael J.; Ulrich, J. Terry; Ward, Jon R.; Cantrell, John L.; Brookshire, Valerie G.
CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribi ImmunoChem Research, Inc., Hamilton, MT, 59840, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(22), 3260
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The name of coauthor Gary L. Gustafson was omitted fro the list of authors' names; the complete list is reprinted.

L11 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:664948 CAPLUS
DOCUMENT NUMBER: 132:26772
TITLE: Monophosphoryl **Lipid A** (MPL) Formulations for the Next Generation of Vaccines
AUTHOR(S): **Baldridge, Jory R.**; Crane, R. Thomas
CORPORATE SOURCE: Ribi ImmunoChem Research, Inc., Hamilton, MT, 59840, USA
SOURCE: Methods (Orlando, Florida) (1999), 19(1), 103-107
CODEN: MTHDE9; ISSN: 1046-2023
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Many of the latest trends in vaccine development are dependent on immunol. adjuvants that mediate and promote a wide variety of immune responses. One promising adjuvant candidate, monophosphoryl **lipid A** (MPL) immunostimulant, is being investigated with many of these new vaccine approaches in either preclin. or clin. trials. This is possible because different vehicle formulations can significantly influence the type of immunol. response MPL promotes. Procedures are provided for formulating MPL in an aq. vehicle or an oil-in-water emulsion. These two MPL formulations can be beneficial for most vaccine approaches being investigated today. (c) 1999 Academic Press.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:663073 CAPLUS
DOCUMENT NUMBER: 132:23151
TITLE: 3-O-Desacyl Monophosphoryl **Lipid A** Derivatives: Synthesis and Immunostimulant Activities
AUTHOR(S): **Johnson, David A.**; Keegan, David S.; Sowell, C. Gregory; Livesay, Mark T.; Johnson, Craig L.; Taubner, Lara M.; Harris, Annalivia; Myers, Kent R.; Thompson, Jennifer D.; Gustafson, Gary L.; Rhodes, Michael J.; Ulrich, J. Terry; Ward, Jon R.; Yorgensen, Yvonne M.; Cantrell, John L.; Brookshire, Valerie G.
CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribi ImmunoChem Research Inc., Hamilton, MT, 59840, USA
SOURCE: Journal of Medicinal Chemistry (1999), 42(22), 4640-4649
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The synthesis of a series of novel analogs of **lipid A**, the active principle of lipopolysaccharide, is reported. In these

compds., the 1-O-phosphono and (R)-3-hydroxytetradecanoyl moieties of native Salmonella minnesota R595 **lipid A** have been replaced with hydrogen and the length of the normal fatty acyl residues has been systematically varied. Normal fatty acid chain length in the 3-O-desacyl monophosphoryl **lipid A** (MLA) series is shown to be a crit. determinant of iNOS gene expression in activated mouse macrophages and the induction of pro-inflammatory cytokines in human peripheral monocytes. Examn. of pyrogenicity in rabbits and lethal toxicity in D-galactosamine-treated mice shows that toxic effects in the MLA series can be ameliorated by modifying fatty acid chain length. When used as an adjuvant for tetanus toxoid vaccines, certain MLA derivs. enhance the prodn. of tetanus toxoid-specific antibodies in mice.

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:536699 CAPLUS
DOCUMENT NUMBER: 131:272113
TITLE: Synthesis and biological evaluation of a new class of vaccine adjuvants: **aminoalkyl glucosaminide** 4-phosphates (**AGPs**)
AUTHOR(S): **Johnson, David A.**; Sowell, C. Gregory; Johnson, Craig L.; Livesay, Mark T.; Keegan, David S.; Rhodes, Michael J.; Ulrich, J. Terry; Ward, Jon R.; Cantrell, John L.; Brookshire, Valerie G.
CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribi ImmunoChem Research, Inc., Hamilton, MT, 59840, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(15), 2273-2278
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel series of acylated .omega.-aminoalkyl 2-amino-2-deoxy-4-phosphono-.beta.-D-glucopyranosides (**aminoalkyl glucosaminide** 4-phosphates) was synthesized and screened for immunostimulant activity. Several of these compds. enhance the prodn. of tetanus toxoid-specific antibodies in mice and augment vaccine-induced cytotoxic T cells against EG.7-ova target cells.
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:796363 CAPLUS
DOCUMENT NUMBER: 130:139549
TITLE: Chemical synthesis of the major constituents of Salmonella minnesota monophosphoryl **lipid A**
AUTHOR(S): **Johnson, David A.**; Sowell, C. Gregory; Keegan, David S.; Livesay, Mark T.
CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribi ImmunoChem Research, Inc., Hamilton, MT, 59840, USA
SOURCE: Journal of Carbohydrate Chemistry (1998), 17(9), 1421-1426
CODEN: JCACDM; ISSN: 0732-8303
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two aminodeoxy glycophospholipids major constituents of Salmonella minnesota were prepd. via coupling of lipids with sugars.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:508532 CAPLUS
DOCUMENT NUMBER: 129:225496
TITLE: Antiischemic effect of monophosphoryl **lipid A** in conscious rabbits with hypercholesterolemia and atherosclerosis
AUTHOR(S): Szilvassy, Zoltan; Ferdinandy, Peter; **Cluff, Christopher W.**; Elliott, Gary T.
CORPORATE SOURCE: First Department of Medicine, Albert Szent-Gyorgyi Medical University, Szeged, Hung.
SOURCE: Journal of Cardiovascular Pharmacology (1998), 32(2), 206-212
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors studied whether monophosphoryl **lipid A** (MLA), an endotoxin deriv., protected the heart from planned ischemia in hypercholesterolemic conscious rabbits. Normal and hypercholesterolemic (8-wk exposure to 1.5% cholesterol-enriched diet) conscious rabbits with right ventricular electrode and left ventricular polyethylene catheters were subjected to ventricular overdrive pacing (VOP; 500 beats/min over 10 min = control VOP). The resulting intracavitary ST-segment elevation, increase in left ventricular end-diastolic pressure (LVEDP), and a redn. of ventricular effective refractory period (VERP) were measured. Three days later the animals were given a single i.v. bolus of 10 or 30 .mu.g/kg MLA or its solvent or both, and a second VOP (test VOP) was applied 24 h later. MLA decreased ST elevation and LVEDP increase from 2.1 .+-. 0.16 to 1.27 .+-. 0.25 and 0.97 .+-. 0.13 mV and 14.6 .+-. 1.2 to 11.1 .+-. 1.0 and 12.4 .+-. 1.2 mm Hg in normal animals and from 2.55 .+-. 0.14 to 1.31 .+-. 0.12 and 0.96 .+-. 0.30 mV and from 21.0 .+-. 1.6 to 11.7 .+-. 1.3 and 12.4 .+-. 1.3 mm Hg in atherosclerotic animals after 10- and 30-.mu.g/kg doses, resp. ($p < 0.001$ for each). VOP-induced VERP redn. was also significantly alleviated by both MLA doses; nevertheless, 30-.mu.g/kg MLA significantly prolonged resting VERP with a slight VERP redn. in response to pacing in both normal and atherosclerotic animals. The authors conclude that MLA produces a delayed antiischemic effect in both normal and hypercholesterolemic/atherosclerotic conscious rabbits.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1997:302174 CAPLUS

DOCUMENT NUMBER: 126:342189

TITLE: Effective adjuvants for the induction of antigen-specific delayed-type hypersensitivity

AUTHOR(S): **Baldridge, Jory R.**; Ward, Jon R.

CORPORATE SOURCE: Ribi ImmunoChem Research, Inc., Hamilton, MT, 59840, USA

SOURCE: Vaccine (1997), 15(4), 395-401
CODEN: VACCDE; ISSN: 0264-410X

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vaccines utilizing poorly immunogenic subunit antigens are dependent upon adjuvants to drive the appropriate T cell responses. In an effort to det. the ability of several adjuvants to promote cell-mediated immunity (CMI), we assessed delayed-type hypersensitivity (DTH) in mice inoculated with heat-killed Listeria monocytogenes (HKLM) vaccines. The vaccines were formulated as oil-in-water emulsions contg. one or more of the following bacterial-derived immunostimulators: MPL immunostimulant, a monophosphoryl **lipid A** prepn., synthetic trehalose dicorynomycolate (TDCM) and Mycobacterium phlei cell wall skeleton (CWS). Oil-in-water emulsions contg. HKLM without adjuvants did not induce DTH responsiveness in mice. The incorporation of TDCM, or MPL plus TDCM and/or CWS to the formulation enabled the HKLM vaccine to stimulate CMI characterized by DTH responsiveness. Following antigen challenge the resulting increases in footpad thickness ranged from 15-20% and were comparable to the DTH driven by complete Freund's adjuvant. Adjuvants composed of MPL/TDCM and MPL/TDCM/CWS induced responses equiv. to those measured in mice immunized with viable L. monocytogenes, and the responses remained at these levels for at least 2 mo. Furthermore, in vivo depletion of CD4+ T cells, but not CD8+ T cells, abrogated the induction and expression of DTH, indicating that the response is mediated by CD4+ T cells.

L11 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:763224 CAPLUS

DOCUMENT NUMBER: 126:131266

TITLE: Efficient asymmetric synthesis of (R)-3-hydroxy- and alkanoyloxytetradecanoic acids and method for the determination of enantiomeric purity

AUTHOR(S): Keegan, David S.; Hagen, Steven R.; **Johnson, David A.**

CORPORATE SOURCE: Pharmaceutical Discovery Div., Ribi ImmunoChem Res., Inc., MT, 59840, USA

SOURCE: Tetrahedron: Asymmetry (1996), 7(12), 3559-3564
CODEN: TASYE3; ISSN: 0957-4166

PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An efficient synthesis of the (R)-3-hydroxy- and alkanoyloxytetradecanoic acid components of bacterial **lipid A** has been achieved using a Ru(II)-Binap-catalyzed low-pressure hydrogenation of

Me(CH2)10COCH2CO2Me. The enantiomeric purity of(R)-Me(CH2)10CH(OH)OCH2CO2CH2COC6H4Br-4 could be assessed directly by chiral HPLC, obviating sep. derivatization steps and/or chiral NMR shift studies.

L11 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1996:412265 CAPLUS
TITLE: Synthesis and immunostimulant activities of monophosphoryl **lipid** a derivatives
AUTHOR(S): **Johnson, David A.**; Keegan, David S.; Sowell, C. Gregory; Livesay, Mark T.; Cantrell, John L.; Ulrich, J. Terry
CORPORATE SOURCE: Pharmaceutical Discovery Division, Ribi ImmunoChem Research, Inc., Hamilton, MT, 59840, USA
SOURCE: Book of Abstracts, 212th ACS National Meeting, Orlando, FL, August 25-29 (1996), CARB-037. American Chemical Society: Washington, D. C.
CODEN: 63BFAF
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB In addn. to their capacity to induce toxic reactions such as fever and lethal shock, bacterial lipopolysaccharide (**LPS**) and its endotoxic principle **lipid A** can have beneficial effects including the enhancement of non-specific immune responses against tumor cells and microbial pathogens. As part of a program aimed at developing synthetic immunostimulants possessing a better balance between beneficial and endotoxic effects, we have prepd. synthetic subunit analogs of S. minnesota **lipid A**. Synthetic methodol. for the efficient construction of the 3-O-desacyl monophosphoryl **lipid A** deriv. shown and related compds. will be presented together with a discussion of their antitumor effects.

L11 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:317763 CAPLUS
DOCUMENT NUMBER: 122:103470
TITLE: Soluble CD14 truncated at amino acid 152 binds lipopolysaccharide (**LPS**) and enables cellular response to **LPS**
AUTHOR(S): Juan, Todd S.-C.; Kelley, Michael J.; **Johnson, David A.**; Busse, Leigh A.; Hailman, Eric; Wright, Samuel D.; Lichenstein, Henri S.
CORPORATE SOURCE: Amgen Inc., Thousand Oaks, CA, 91320, USA
SOURCE: Journal of Biological Chemistry (1995), 270(3), 1382-7
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CD14 is a 55-kDa glycoprotein which binds lipopolysaccharide (**LPS**) and enables **LPS**-dependent responses in a variety of cells. To identify the domains in CD14 required for function, the authors deleted increasing amts. of CD14 from the C-terminus. Truncated CD14 cDNA sequences were transfected into COS-7 cells and serum-free conditioned medium was analyzed for mutant CD14 expression and bioactivity. Mutant CD14s contg. as few as 152 amino acids were found to have activity equiv. t.omega. full length sCD14. To further characterize the mutant CD14, the authors constructed a stable Chinese hamster ovary cell line expressing sCD141-152 and purified the protein to homogeneity. The sCD141-152 bound radioactive **LPS**, enabled U373 cells to synthesize interleukin 6 in response to **LPS**, and enabled human neutrophils to respond to smooth **LPS**. In all of these assays, the behavior of sCD141-152 was quant. similar to full-length sCD14. The authors also found that two neutralizing anti-CD14 antibodies (3C10 and MEM-18) bound and neutralized sCD141-152. The authors conclude from these expts. that the N-terminal 152 amino acids of CD14 are sufficient to bind **LPS** and confer essentially wild-type bioactivity in vitro.

L11 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:74995 CAPLUS
DOCUMENT NUMBER: 120:74995
TITLE: Lipopolysaccharide (**LPS**)-binding protein accelerates the binding of **LPS** to CD14
AUTHOR(S): Hailman, Eric; Lichenstein, Henri S.; Wurfel, Mark M.; Miller, David S.; **Johnson, David A.**; Kelley, Michael; Busse, Leigh A.; Zukowski, Mark M.; Wright, Samuel D.
CORPORATE SOURCE: Lab. Cell. Physiol. Immunol., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1994), 179(1),

269-77
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CD14 is a 55-kD protein found as a glycosylphosphatidylinositol (GPI)-anchored protein on the surface of monocytes, macrophages, and polymorphonuclear leukocytes, and as a sol. protein in the blood. Both forms of CD14 participate in the serum-dependent responses of cells to bacterial lipopolysaccharide (**LPS**). While CD14 has been described as a receptor for complexes of **LPS** with **LPS** -binding protein (LBP), there has been no direct evidence showing whether a ternary complex of **LPS**, LBP, and CD14 is formed, or whether CD14 binds **LPS** directly. Using nondenaturing polyacrylamide gel electrophoresis (native PAGE), the authors show that recombinant sol. CD14 (rsCD14) binds **LPS** in the absence of LBP or other proteins. Binding of **LPS** to CD14 is stable and of low stoichiometry (one or two mols. of **LPS** per rsCD14). Recombinant LBP (rLBP) does not form detectable ternary complexes with rsCD14 and **LPS**, but it does accelerate the binding of **LPS** to rsCD14. The rLBP facilitates the interaction of **LPS** with rsCD14 at substoichiometric concns., suggesting that LBP functions catalytically, as a lipid transfer protein. Complexes of **LPS** and rsCD14 formed in the absence of LBP or other serum proteins strongly stimulate integrin function on PMN and expression of E-selectin on endothelial cells, demonstrating that LBP is not necessary for CD14-dependent stimulation of cells. Apparently, CD14 acts as a sol. and cell surface receptor for **LPS**, and LBP may function primarily to accelerate the binding of **LPS** to CD14.

L11 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1987:437707 CAPLUS
DOCUMENT NUMBER: 107:37707
TITLE: An early response to lipopolysaccharide is the elicitation of macrophages specialized for antigen degradation with negative regulatory effects on the induction of specific immune responses
AUTHOR(S): **Cluff, Christopher W.**; Ziegler, H. Kirk
CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA
SOURCE: Infection and Immunity (1987), 55(6), 1346-54
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of macrophages to catabolize antigens is relevant both as a means to process complex antigens before presentation to T cells and as a way to down-regulate immune responses by destroying the antigenicity of polypeptides. With these considerations in mind, the authors investigated the regulation of macrophage catabolic activity by lipopolysaccharide (**LPS**). Catabolic activity was quantitated by following the distribution and mol. form of 125I-labeled surface components of heat-killed Listeria monocytogenes after their uptake by macrophages. The authors compared the catabolic activity of macrophages from peritoneal exudates of mice injected i.p. with saline or **LPS** and found that **LPS**-elicited macrophages displayed a greatly enhanced rate of catabolism. This increase in catabolic activity peaked 3 days after **LPS** injection and slowly declined thereafter, approaching a base-line level after 3 wk. The enhancement of catabolic activity was under **Lps** gene control. Macrophages that were elicited 3 days after i.p. injection of **LPS** rapidly destroyed the antigenicity of bacterial antigens, expressed low levels of Ia mols., and processed and presented antigen slowly when tested as antigen-presenting cells in vitro. An injection of **LPS** before infection with L. monocytogenes resulted in diminished development of T-cell reactivity to this organism. Apparently, **LPS** elicits a macrophage population specialized for antigen degrdn. functions, with neg. regulatory effects on the induction of specific immune responses.